Serum Uromodulin Predicts Graft Failure in Renal Transplant Recipients

Steubl Dominik[1], Block Matthias[2], Herbst Victor[2], Nockher Wolfgang Andreas[3], Schlumberger Wolfgang[2], Angermann Susanne[1], Heemann Uwe[1], Renders Lutz[1], Scherberich Jürgen[4]

[1] Abteilung für Nephrologie, Klinikum rechts der Isar, Technische Universität, München, Germany
[2] Euroimmun Medizinische Labordiagnostika AG, Lübeck, Germany
[3] Institut für Laboratoriumsmedizin und Pathobiochemie, Universitätsklinikum Marburg, Philipps-Universität Marburg, Germany
[4] Klinikum München-Harlaching, Teaching Hospital of the Ludwig-Maximilian-Universität, München, Germany

Background: Serum uromodulin, a protein exclusively secreted in the thick ascending limb of the loop of Henle, was demonstrated to correlate with kidney function in chronic kidney disease patients. This article studies the value of uromodulin for the prediction of graft failure in renal transplant recipients.

Patients&Methods: Serum uromodulin, cystatin C, creatinine and urea-nitrogen (BUN) concentrations and eGFR (CKD-EPI$_{creatinine/cystatin\ C}$) were assessed one to three months after transplantation in 91 patients when transplant function had stabilised. Multivariate cox regression analysis and receiver-operating-characteristic (ROC) curve were used to analyse the predictive value of all parameters concerning graft loss (GL).

Results: Follow-up time was 3.6±2.2 years. Uromodulin was moderately associated with estimated glomerular filtration rate (eGFR) in multivariate linear regression modelling (r=0.330, p<0.001, figure 1). In cox regression analysis uromodulin predicted GL equivalently to the other markers studied (table 1): the risk for GL was reduced by 0.21 per one standard deviation increase (SD) of uromodulin (cystatin C: HR 4.57, creatinine: HR 4.53, BUN: HR 2.50, eGFR: HR 0.10 per increase of one SD). In ROC analysis, uromodulin predicted GL with an area-under-the curve of 0.782 [p=0.001, 0.623-0.942] at an optimal cut-off of 24.0 ng/ml with a sensitivity of 90.0% and a specificity of 70.2%; similar results were found for the other parameters tested (table 2).

Conclusions: Serum uromodulin, a marker of tubular integrity and function, predicted GL equivalently compared to conventional biomarkers of glomerular filtration. These findings suggest that deterioration of graft function can be assessed using both markers of glomerular filtration AND tubular function. Tubular function appears to play an important role for long term renal allograft survival.

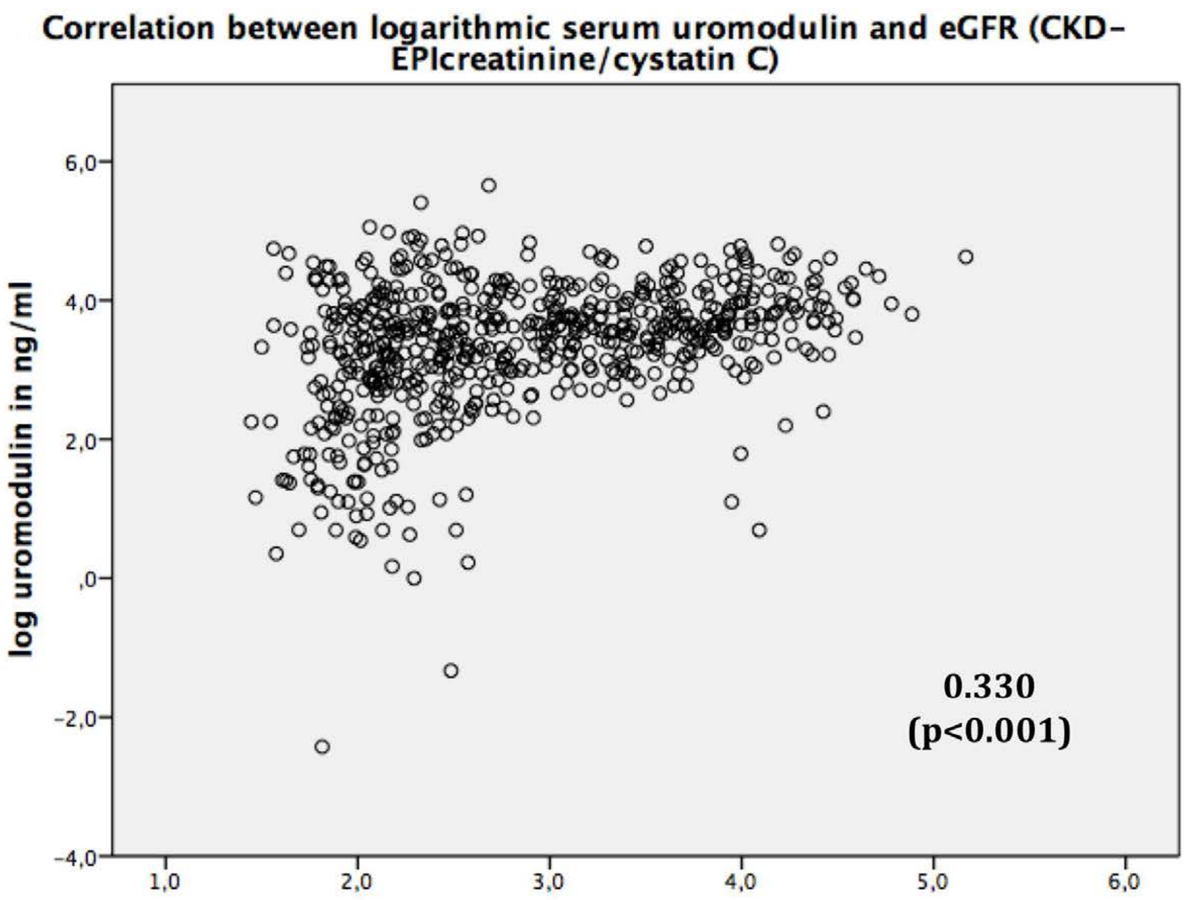

Figure 1: Scatterplot showing the multivariate linear regression modelling between log serum uromodulin and log eGFR (CKD-EPI$_{creatinine/cystatin\ C}$); ng/ml = nanogram per milliliter; mg/dl = microgram per deciliter

Table 1: Multivariate cox regression analysis evaluating the association of predictors and graft loss

Biomarker/eGFR	Patients EP reached	Patients EP not reached	HR (95% CI)	Calulated HR for one SD	p-value
Graft loss	**13**	**78**			
Uromodulin (ng/ml)	*30.6±23.7*	*50.9±24.6*	***0.940 (0.900-0.981)***	***0.21***	***0.005***
Cystatin C (in mg/l)	*3.2±1.7*	*1.6±0.8*	***3.981 (2.213-7.163)***	***4.57***	***<0.001***
Creatinine (in mg/dl)	*3.7±2.2*	*1.9±1.3*	***2.572 (1.675-3.947)***	***4.53***	***<0.001***
BUN (in mg/dl)	*49.2±24.2*	*32.5±15.0*	***1.054 (1.023-1.086)***	***2.50***	***0.001***
eGFR (CKD-EPI, in ml/min)	*25.7±21.8*	*50.5±26.5*	***0.918 (0.873-0.967)***	***0.10***	***0.001***

EP = endpoint; HR = hazard ratio for elevation of 1 unit per biomarker, e.g. 1 ng/ml of uromodulin and 1mg/dl for creatinine; SD = standard deviation; calculated HR for one SD = SD of whole cohort used; CI = confidence interval; BUN = blood-urea-nitrogen; eGFR = estimated glomerular filtration rate;

Table 2: Receiver-operating-characteristic curve for the prediction of graft loss (n=13)

Biomarker/eGFR	AUC (p-value)	95%-CI	Optimal cut-off (unit)	Sensitivity (%)	Specifity (%)
Uromodulin (ng/ml)	***0.782 (0.001)***	***[0.623-0.942]***	***24.0***	***90.0***	***70.2***
Cystatin C (in mg/l)	***0.763 (0.002)***	***[0.581-0.945]***	***2.5***	***69.2***	***88.7***
Creatinine (in mg/dl)	***0.778 (0.001)***	***[0.625-0.932]***	***2.1***	***76.9***	***73.8***
BUN (in mg/dl)	***0.756 (0.003)***	***[0.641-0.870]***	***34.5***	***76.9***	***66.2***
eGFR (CKD-EPI, in ml/min)	***0.794 (0.001)***	***[0.639-0.949]***	***22.4***	***86.3***	***69.2***

BUN = blood urea nitrogen; eGFR = estimated glomerular filtration rate; AUC = area under the curve; CI = confidence interval;

Dr. med. Dominik Steubl, Department of Nephrology , Klinikum rechts der Isar, Ismaninger Str. 22, D-81675 München, Germany
Phone: ++49-89-4140-2231 - Fax: ++49-89-4140-4878 - dominik.steubl@gmx.de
Copyright © 2016

53 ERA 669-SP
Renal transplantation. Clinical.
Dominik Steubl
DOI: 10.3252/pso.eu.53era.2016
ePosters supported by F. Hoffmann- La Roche Ltd.
53rd CONGRESS ERA-EDTA VIENNA AUSTRIA MAY 21st-24th 2016
Hold jointly with Österreichische Gesellschaft für Nephrologie
PosterSessionOnline.com